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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/702,525	02/07/97	SHARPE	A BM1-1200PLS
LAHIVE & COOKFIELD, LLP 28 STATE STREET BOSTON MA 02109		HM11/1208	EXAMINER
			GAMBEL, P
		ART UNIT	PAPER NUMBER
		1644	14
DATE MAILED: 12/08/98			

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

Responsive to communication(s) filed on 9/11/98

This action is FINAL.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

Claim(s) 1-77 is/are pending in the application.  
Of the above, claim(s) 18-29, 32, 48-59, 62, 66-68, 73-74 is/are withdrawn from consideration.

Claim(s) \_\_\_\_\_ is/are allowed.

Claim(s) 1-(2, 30-31, 33-47, 60-61, 63-65, 69-71, 75-77 is/are rejected.

Claim(s) \_\_\_\_\_ is/are objected to.

Claims \_\_\_\_\_ are subject to restriction or election requirement.

**Application Papers**

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All  Some\*  None of the CERTIFIED copies of the priority documents have been received.

received in Application No. (Series Code/Serial Number) \_\_\_\_\_

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

Notice of Reference Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

### **Detailed Action**

1. The location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1644, Technology Center 1600.

2. Applicant's amendment, filed 9/21/98 (Paper No. 13), is acknowledged.

Claims 1-17, 33-47, 63-71, and 77 have been amended.

Claims 1-17, 30-31, 33-47, 60-61, 63-65, 69-71 and 75-77 are under consideration.

Claims 18-29, 32, 48-59, 62, 66-68, 73-74 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

3. Applicant's IDS, filed 7/14/97 (Paper No. 7) is acknowledged, however the 1449 could not be located in the application. Therefore, the reference provided were cited on a PTOL 892.

4. The drawings submitted with this application were declared informal by the applicant. Accordingly, they have not been reviewed by draftsperson at this time. When formal drawings are submitted, the draftsperson will perform a review.

Direct any inquiries concerning drawing review to the Drawing Review Branch (703) 305-8404.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the <sup>TM</sup> or <sup>®</sup> symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

6. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action. This Office Action will be in response to applicant's arguments, filed 9/21/98 (Paper No. 13). The rejections of record can be found in the previous Office Action (Paper No. 13).

7. Upon reconsideration and in view of applicant's amended claims and arguments, filed 9/21/98 (Paper No. 13); the previous rejection as it applies to the instant claims under 35 U.S.C. § 112, first paragraph, new matter has been withdrawn.

8. Claims 1-17, 30-31, 33-47, 60-61, 63-65, 69-71 and 75-77 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments, filed 9/21/98 (Paper No. 13), have been fully considered but are not found convincing essentially for the reasons of record set forth in Paper No. 11.

Applicant argues that the instant claims are directed to novel nucleic acid molecules which are naturally occurring variants of the nucleotide sequences shown in SEQ ID NOS. 18/22, which are alternative splice forms of prior art B7-1/B7-2 molecules. Applicant's reliance on art known domains and amino acid positions is acknowledged. Applicant argues that the claims provide for sufficient structural information and defining characteristics which would be readily understood by the ordinary artisan. Further applicant argues that the claims require that the subject alternatively spliced forms of B7-1/B7-2 molecules meet certain structural limitations. Therefore, the claims only embrace B7-1 and B7-2 nucleic acid molecules which encode functional T cell costimulatory molecules and do not read on inoperative species. Applicant's arguments concerning enablement, including that once a putative alternative structural domain or novel exon has been identified, the nucleotide sequence encoding the domain can be mapped in genomic DNA to determine whether the domain is encoded by a novel exon, are acknowledged.

It is acknowledged that the claims provide certain structural and functional characteristics of the claimed B7-1/B7-2 encoding nucleic acids. Again, while these characteristics may have some notion of the specificity and structure of the nucleic acids, these claims lack sufficient structural information or defining characteristics which distinctly claim all of the known and unknown nucleic acids encoding any alternative spliced or naturally occurring variant, including the various elements (e.g. exons, domains), encompassed by the claimed invention. Although the claims have been amended to provide more structure and function; the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the ill-defined number of known and unknown nucleic acids broadly encompassed by the claims. The instant specification discloses a limited number of alternative spliced or naturally occurring forms of costimulatory molecules. In addition, applicant has not provided sufficient biochemical information (e.g. sequence) that distinctly identifies all of the known and unknown alternatively spliced variants encompassed by the claimed nucleic acids. Also, the claims recites negative limitations with respect to other known nucleic acids encoding B7-1 or B7-2, however there is insufficient guidance and written description for the breadth of the claimed nucleic acids. Predicting structural determinations to ascertain functional aspects of the nucleic acids to encode functional protein which bind CD28 and CTLA-4 and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation. Again, the claims are not even limited to clearly defined number of nucleic acids encoding alternatively spliced or naturally occurring variants of B7-1/B7-2 nucleic acid encoding, but further extend to an ill-defined number of species which share one or more functional or structural characteristics with the known B7-1 or B7-2 molecules.. As the specification does not teach how to make or use a number of species that would be commensurate in scope with the claims, it is found that it would require undue experimentation practice the invention in a manner commensurate in scope with the claims.

It was found in Amgen v. Chugai, 18 USPQ 2d 1017 at 1021, that: "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. See Oka, 849 F. 2d at 583, 7 USPQ2d at 1171. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method or preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having nor more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, *i.e.*, until after the gene has been isolated."

This position was further supported in Fiers v. Sugano, where it was stated: "An adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself" (26 USPQ2d 1601 at 1606). Thus, the instant specification does not adequately describe, and therefore *cannot* adequately teach how to make, the claimed invention.

"It is not sufficient to define the recombinant molecule by its principal biological activity, e.g. having protein A activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property." Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992).

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the isolated nucleic acids in manner reasonably correlated with the scope of the claims broadly including any number of additions, deletions, insertions or substitutions of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made in the nucleic acids encoding a protein's structure and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

Applicant's arguments are not found persuasive.

9. Upon reconsideration including consideration of applicant's arguments and amended claims, filed 9/21/98 (Paper No. 13), that the instant claims do not read on known B7 molecules in the prior art; the previous rejections as they would apply to the instant claims under 35 U.S.C. § 102(a)(b) as being anticipated by Freeman et al. (J. Exp. Med. 174:625-631, 1991), Selvakumar et al. (Immunogenetics 36:175-181, 1992), Selvakumar et al. (Immunogenetics 38:292-295, 1993), Freeman et al. (J. Immunol. 143:2714-2722, 1989), Freeman et al. (J. Exp. Med. 178:2185-2192, 1993) or Freeman et al. (Science. 262:909-911, 1993) as well as under 35 U.S.C. § 103 as being unpatentable over any of Freeman et al. (J. Exp. Med. 174:625-631, 1991), Selvakumar et al. (Immunogenetics 36:175-181, 1992), Selvakumar et al. (Immunogenetics 38:292-295, 1993), Freeman et al.(J. Immunol. 143:2714-2722, 1989), Freeman et al. (J. Exp. Med. 178:2185-2192, 1993), Freeman et al. (Science. 262:909-911, 1993) or Azuma et al. (Nature 366:76-77, 1993).

10. No claim is allowed.

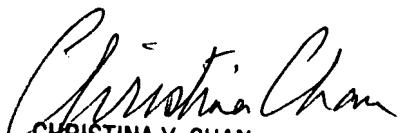
11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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December 3, 1998



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